REMARKS

Claims 1-2, 5, 7-16, 18-21, and 43, appear in this application for the Examiner's consideration. Claims 1, 2, 5, 21 and 43 have been amended. Claim 4, 6 and 41-42 have been cancelled. Claims 22-40 are currently withdrawn from consideration but it is understood that these claims will be rejoined when claim 1 is allowed, since they all ultimately depend from claim 1.

Regarding claim changes, claim 1 has been amended to further define the desired porosity range. Specifically, the porosity was amended from "a desired porosity" to "a desired porosity of about 87 +/-SD 1.5% to about 94 +/-SD 0.1%." Support for this amendment can be found in Example 1, on page 20, lines 4-6 of the present application, reciting "(t)he addition of glycerol resulted in a reduction in the porosity to 94% ± 0.1. A further significant decrease to values of 90% ± 1.3, 88% ± 1 and 87% ± 1.5 was observed following the addition of bentonite, kaolin and chitin, respectively." Claim 1 has also been amended to incorporate the features recited in the cancelled claim 4.

Claim 2 has been amended to correct confusing language. Specifically, the phrase "entrapped of the freeze-dried bead" was replaced with "entrapped in the freeze-dried bead."

Claim 5 has been amended to depend from claim 2 instead of the cancelled claim 4.

Claim 21 has been amended to more accurately present the range of the bead diameters. Specifically, the range was changed from "between several microns to 4mm" to "from 50 microns to 500 microns." Support for this amendment can be found on page 3, lines 28-29 of the present application, reciting "(p)referably, the size of the beads is between 50 microns to 500 microns."

Claim 43 has been amended to more accurately present the range of the average thickness of the pore walls by removing the thickness of the pore walls of the control from the range. Specifically, the range of the thickness of the pore walls was amended from "an average thickness of about 1.47 micrometers to about 11.43 micrometers" to "an average thickness of about 1.55 micrometers to about 11.43 micrometers." Support for this amendment can be found in Example 1, on page 19, lines 12-15 of the present application, where it states that, "(a)ddition of glycerol, chitin, bentonite or kaolin to the beads increased bead thickness ~ 1.5- to 3-fold. Beads entrapping glycerol and a filler had a significantly thicker wall, with alginate-glycerol-kaolin beads having the thickest walls (11.43 μm) (Table

1)" and in Table 1 on page 20 of the present application, wherein values for thickness of the pore walls ranging from 1.55 micrometers to 11.43 micrometers are provided.

Claim 43 has been further amended to correct the description of the "walls" separating the pores. Specifically, the phrase "includes pores separated by pore walls" has been replaced with, "includes pores separated by bead walls". Support for this amendment, can be found on page 7, line 18 of the present application, reciting "(f)igure 5 shows SEM of typical freeze-dried alginate beads walls", in Example 1 on page 19, lines 9-11 of the present application, where it states, "(t)o understand the connection between bead wall thickness and protection against UVC, the wall thickness of cross-sectioned freeze-dried alginate beads was measured," and in Table 1 on page 20 of the present application.

Since no new matter is introduce by these changes, they all should be entered at this time to reduce the issues for appeal by in general overcoming the rejections and in particular placing the application in condition for allowance.

Claims 21, 42 and 43 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In response, claims 21 and 43 have been amended as explained above and claim 42 has been cancelled. Thus the rejection has been overcome and should be withdrawn.

Claims 2, 21, 41 and 43 are rejected under 35 U.S.C. § 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In response, claims 2, 21 and 43 have been amended as explained above and claim 41 has been cancelled. Thus the rejection has been overcome and should be withdrawn.

Claims 1, 2, 4-13, 16, 18-21 and 41-43 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 4,818,530 to Marois et al (referred to hereafter as "Marois") in view of U.S. Patent No. 4,956,295 to Sudoma (referred to hereafter as "Sudoma"). Marois teaches pelletization of fungal spores for use in biocontrol and discloses that pelletization of the alginate requires calcium salt and gelation proceeds faster as the concentration of the salt solution is increased. Sudoma teaches the stabilization of dried bacteria in particulate carriers. Neither Marois nor Sudoma teaches the present invention of porous dried beads to be stored at low temperatures for a long period of time. In particular, Marois at column 5 lines 15-17 states "(d)rying transformed the gel beads into hard granules

or pellets which were stored under room conditions." Sudoma is directed to the combination of dried viable bacteria with particulate carriers to form highly diluted admixtures storable without refrigeration.

In contrast, the present invention specifically teaches the unexpected benefits of providing a high degree of porosity and increased viability for a period of years upon storage at or below -18°C after freeze drying with cryoprotection. Specifically, there would have been no way to anticipate prolonged viability (12-36 months) in the absence of the findings reported in on page 4, lines 20-29 of the present invention,

> "In preferred embodiments wherein the dried cellular solid carriers comprise glycerol not less than 50% of the microorganisms remain viable for at least one year of storage at temperatures below -18°C. Preferably, not less than 75% of the microorganisms remain viable for at least one year of such storage and most preferably, around 90% to 95% or more of the microorganisms remain viable for at least one year of such storage. Furthermore, preferred embodiments include retention of these proportions of microorganism viabilities for at least 2 to three years of storage as dried beads at temperatures at or below -18°C. If desired, lower storage temperatures to as low as -70°C can be used to maintain microorganism viabilities for longer storage times."

This extraordinary viability over years of storage is a new and non-obvious result. In Marois, on the other hand, the majority of the microorganisms of the examples died within 12 weeks. In fact, 12 weeks was the upper limit measured in Marois (Table1). Viability of the entrapped microorganisms within a hydrocolloid bead for a period of years (12-36 months) was never taught, suggested or even aspired to by Marois.

Sudoma refers to the use of cryoprotectants as an additive to facilitate the preparative drying process of the isolated bacteria themselves (col. 5, ll. 21-25), which has been known for decades prior to Sudoma (see col. 3, ll. 18-30). Sudoma does not disclose and cannot be inferred to predict the use of a cryoprotectant to maintain the viability of organisms entrapped within a hydrocolloid gel (or to achieve a desired level of porosity). Sudoma's use of a cryoprotectant would therefore not overcome the deficiencies of Marois as one of skill in the art combining Marois with Sudoma could only arrive at a combination of viable dried bacteria within a hydrocolloid gel and not a freeze dried porous hydrocolloid gel containing viable microorganisms.

Furthermore, Sudoma is directed to compositions of dried bacteria with inorganic salts and a small proportion of water absorbing silica gel to produce a "highly diluted admixture," suitable to storage without refrigeration. Sudoma states, "A number of common inorganic salts have been found particularly desirable, such as the sodium, potassium or calcium carbonates, bicarbonates, sulfates, and phosphates." (see col. 3, ll. 67-68 and col. 4, ll. 1-2). Sudoma further discloses that the mixture must include silica gel absorbent for freeze-drying the cells prior to storage. The use of silica gel is made inherently necessary by the fact that these preferred salts, such as calcium salt, have no known applicability to hydrocolloid gel. Unlike Sudoma, the present application does not seek compositions suitable for storage without refrigeration but rather prolonged viability (12-36 months) during long-term storage at or below minus 18°C.

Moreover, none of the ingredients considered necessary in the present application for successfully enhancing long-term viability are found in Sudoma. Specifically, glycerol is not in any way suggested as a suitable cryoprotectant in Sudoma, since glycerol is a liquid at room temperature. Furthermore, teachings of Sudoma could not have been considered relevant to the claims of the present application which is based on hydrocolloid gels, which are organic polymers completely distinct from any of the materials taught or suggested by Sudoma.

Even if one would have used the freeze-drying, as suggested by Sudoma, on pellets of Marois, it could not have been foretold that the resultant pellets would inherently be porous, after the freeze-drying, to the extent that the pellets would inherently have a porosity between 87 +/-SD 1.5% and 94 +/-SD 0.1%, as recited in claim 1 as amended and a bead wall thickness between about 1.55 and 11.43 micrometers, as recited in claim 43, as amended. Thus, it was not obvious that freeze drying would or could maintain the viability of the entrapped microorganisms or achieve desired porosity.

In this application, therefore, it is the freeze drying of a hydrocolloid gel combined with cryoprotectant and storage at or below -18°C, that permits not only successful drying but also facilitates a high viability rate for the entrapped micro-organisms and the achievement of a desired level of porosity. These advantages of the present invention could not have been foreseen or derived from the combination of Marois and Sudoma, since these

two references neither foresee the benefit of the porous freeze-dried beads of the present invention nor provide methods suitable to achieving it.

Claims 14 and 15 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Marois in view of Sudoma and further in view of U.S. Patent No. 5,030,562 to Elliott et al. (referred to hereafter as "Elliott") or U.S. Patent No. 4,764,371 to Pusey et al. (referred to hereafter as "Pusey"). Elliot teaches a method of screening for bacterial strains which can inhibit the growth and spread of a species of weed that compete with crops while Pusey teaches post harvest control of brown rot on stone fruit.

As explained previously, Marois and Sudoma do not teach the porous freeze-dried beads of the present invention. Neither Elliot nor Pusey remedies this deficiency. Thus, Elliot and Pusey would not have any bearing on this application, whether the pellets contained bacteria or fungi.

Even assuming that the pellets of Marois would be freeze-dried as suggested for the bacteria of Sudoma, however, it would not have been obvious to replace the fungi in the pellets that control a soilborne disease in Marois with bacteria that control a plant pathogen, as suggested by Elliott or Pusey. Moreover, in Pusey, the test bacteria are directly applied to the surface of the fruit and, therefore, Pusey teaches away from applying the bacteria to the soil or plants (see col. 2, lines 41-51). Thus, it is unlikely that a skilled artisan would even be motivated to combine Marois and Pusey to obtain the invention defined by claims 14-15.

In summary, it is completely unfounded to assert that the outcome of freeze drying of hydrocolloid gel beads containing microorganisms with cryoprotectants would inherently have given the present results, since such a combination to provide a desired porosity was never sought in the prior art. There is no teaching or suggestion in the art that predicts that freeze drying of gels with microorganisms and a cryoprotectant would give porous gels which provide a very high level of viable microorganisms over prolonged periods of storage in the frozen state (a period of years).

Therefore, none of the cited references, alone or in combination, teaches solid porous cellular hydrocolloid carriers comprising freeze-dried hydrocolloid beads comprising viable microorganisms entrapped therein. Thus, the obviousness rejection of claims 14-15 under 35 U.S.C. § 103(a) should be withdrawn.

In view of the above, it is respectfully submitted that all current rejections have been overcome and should be withdrawn. Accordingly, the entire application is believed to be in condition for allowance, early notice of which would be appreciated. Should the Examiner not agree, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of this application.

Respectfully submitted,

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